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| APPLICATION NO.                        | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/602,489                             | 06/23/2003  | Ian David Manger     | FI31.K1.US          | 1122             |
| 35341                                  | 7590        | 04/03/2007           | EXAMINER            |                  |
| FLUIDIGM CORPORATION                   |             |                      | HYUN, PAUL SANG HWA |                  |
| 7000 SHORELINE COURT                   |             |                      | ART UNIT            | PAPER NUMBER     |
| SUITE 100                              |             |                      | 1743                |                  |
| SOUTH SAN FRANCISCO, CA 94080          |             |                      |                     |                  |
| SHORTENED STATUTORY PERIOD OF RESPONSE |             | MAIL DATE            | DELIVERY MODE       |                  |
| 3 MONTHS                               |             | 04/03/2007           | PAPER               |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

|                              |                 |               |
|------------------------------|-----------------|---------------|
| <b>Office Action Summary</b> | Application No. | Applicant(s)  |
|                              | 10/602,489      | MANGER ET AL. |
|                              | Examiner        | Art Unit      |
|                              | Paul S. Hyun    | 1743          |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 10 January 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-15 and 18-33 is/are pending in the application.
- 4a) Of the above claim(s) 1-13,32 and 33 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 14,15 and 18-31 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 23 June 2003 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date: _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/14/06</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: _____                          |

Art Unit: 1743

**DETAILED ACTION**

**REMARKS**

Claims 1-15 and 18-32 are currently pending. Claims 1-13, 32 and 33 remain withdrawn in accordance to the restriction requirement imposed on 06/06/06. Therefore, only claims 14, 15 and 18-31 will be considered on the merits.

Applicants amended claims 14 and 28. The amendment to claim 28 overcame the 35 U.S.C. section 112 rejection cited in the previous Office action. Therefore, the rejection has been withdrawn. The amendments to claim 14 have changed the scope of claims 14, 15 and 18-31. Nonetheless, the art rejections cited in the previous office action are maintained.

***Information Disclosure Statement***

The information disclosure statement filed on 14 December 2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

***Drawings***

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the reference numbers and the details of the informal drawings are hard to see. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer

prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

**Claims 14, 15, 18-22, 28-30** are rejected under 35 U.S.C. 102(e) as being anticipated by Van Dam et al. (US 2003/0008411 A1).

Van Dam et al. disclose a microfluidic device and a method for synthesizing a library of compounds by using the microfluidic device (see claim 15), which includes DNA synthesis (see [0056]). The device comprises a solid substrate layer and an elastomeric layer attached to the solid substrate wherein the surface of the solid substrate bonded to the elastomeric layer is immobilized with ligands for binding analytes of interest. The surfaces of both layers can comprise grooves/wells to define a plurality of first flow channels intersecting a plurality of second flow channels (see claim 24 and [0048]). The device further comprises a plurality of control channels associated with each of the flow channels. Upon the application of an actuation force within the control channels, the elastic surface of the control channels deflect into the flow

channels and block fluid flow through the flow channels. The control channels also act as a pump for facilitating the movement of fluids through the flow channels (see [0068] and [0069]).

The method comprises the steps of introducing a reagent into the first flow channels such that the reagent binds to the ligands immobilized to the surface of the solid substrate, and then introducing a sample solution into the second flow channels such that the sample in the sample solution circulates through the flow channels and binds the reagents bound to the immobilized ligands (see claims 25 and 26). The reference discloses that the limitation "reagent" refers to oligonucleotides, peptides, monomers, and other small molecules that are building blocks of a larger molecule (see [0056]). While the fluid is being introduced into one of the two flow channels, the other set of flow channels is closed off by means of the control valves in order to prevent cross-contamination (see [0089]). The reference also discloses that reagents/samples that do not bind to the substrate are rinsed off using a solvent (see [0084]). The efficacy of the binding is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence (see [0122]).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-26 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al.

Van Dam et al. does not explicitly disclose 1) actuating all the control valves to allow the reagent and the sample to incubate; 2) the usage of a detector to observe the compound synthesis; or 3) conducting an assay involving antimicrobes.

Although the Van Dam et al. reference does not explicitly disclose the step of actuating all the valves in order to allow the reagent and the sample to thoroughly react, it is well known in the art to allow reactions to incubate, especially for synthesis reactions such as PCR. It would have been obvious to one of ordinary skill in the art to actuate all the valves after the introduction of the sample in the method disclosed by Van Dam et al. so that the reaction between the reagent and the sample can thoroughly proceed.

Although the Van Dam et al. reference does not explicitly disclose the step of using a detector to observe the reaction product, the reference does disclose the step of derivatizing the solid substrate and determining the efficacy of the derivatization (see [0122]). This is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence. In light of the disclosure, it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method disclosed by Van Dam et al. and detect the fluorescence using a fluorescent microscope in order to observe the efficacy of the synthesis.

Although the Van Dam et al. reference does not explicitly disclose an assay involving antimicrobes, given that the device disclosed by the Van Dam reference is

adapted to perform an assay (binding reagents to ligands), it would have been obvious to one of ordinary skill in the art to react any two entities that bind using the device disclosed by Van Dam et al., including a cell as the reagent and antimicrobes as the sample in order to observe the effects of the antimicrobes on the cell.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. in view of Raillard et al. (US 2002/0102577 A1).

Van Dam et al. does not explicitly disclose the usage of a non-optical detector to observe the compound synthesis. However, the Van Dam et al. reference discloses the step of derivatizing the solid substrate and determining the efficacy of the derivatization (see [0122]). This is accomplished by labeling the functional groups that are attached to the solid substrate with fluorophores and detecting the fluorescence.

Raillard et al. disclose a method for labeling probes with radio-isotopes that emit radiation (see [0132]). The probe is detected using a detector that is sensitive to radiation.

In light of the disclosure of Raillard et al., it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method disclosed by Van Dam et al. with radio-isotope probes instead of fluorophores and detect the radiation using a detector in order to observe the efficacy of the synthesis in the event that fluorophores are not available.

***Response to Arguments***

Applicant's arguments with respect to the art rejections have been fully considered but they are not persuasive. Specifically, Applicants' argument that the Van Dam et al. reference does not disclose the step of re-circulating the sample solution within the flow channels is not persuasive. First, it should be noted that claim 14 does not recite what is alleged by Applicants in the Remarks/Arguments. Applicants argue that the amended claim 14 recites that the sample fluid is re-circulated through each flow channel. However, the claim merely recites that the sample solution is circulated through the flow channels such that anti-ligands in the sample solution may sufficiently bind the immobilized ligands in the flow channel, which is disclosed by Van Dam et al. as discussed in the maintained art rejection. Second, even if Applicants did explicitly recite that the sample solution is circulated through the sample channels multiple times, Van Dam et al. disclose that in complicated reaction sequences, a plurality of valves at the waste side of the device can be configured to redirect the flow from selected channels back into other channels flowing in the reverse direction (see [0190]). The disclosure sufficiently anticipates the newly added limitation as alleged by Applicants.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul S. Hyun whose telephone number is (571)-272-8559. The examiner can normally be reached on Monday-Friday 8AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PSH  
3/27/07

  
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